

Dear Editor,

Thanks for the opportunity to revise and submit this manuscript to *World Journal of Clinical Cases*. We have now addressed the reviewers' comments in full, and point-by-point responses are appended below. Furthermore, the revisions are highlighted in the revised version of the manuscript.

An updated editing certificate is also attached.

We hope that it is now suitable for publication.

Yours sincerely

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Point-by-point responses to the reviewers' comments from peer-review report

Responses to Reviewer 1

The manuscript is overall well written. However, I think the scientific quality of this case report is insufficient for consideration of publication in WJG.

*We modified the articles according to the reviewers' comments and transferred to *World Journal of Clinical Cases*, according to editor's suggestion.*

Responses to Reviewer 2

1). This case report was well written, but myocarditis in UC was not very rare. What was the possibility of mesalamine inducing myocarditis?

Thank you for your positive feedback and questions. The patient had used mesalamine (3 g/day) as maintenance therapy for 1 year before myocarditis without any adverse reactions. Therefore, the possibility of mesalamine inducing myocarditis is nearly impossible. We have clarified this in the revised text.

2) Was that first intake 2 weeks before fever and chest pain. Usually, intolerant symptoms occurs in 7-10 days from mesalamine initiation. Please describe the treatment and clinical course of UC.

We have refined the description of the history of past and present illness. The patient had used mesalamine (3 g/day) as maintenance therapy for 1 year before myocarditis, as shown below and as clarified in the revised text:

UC maintenance therapy	Mesalamine (3 g/day)
When gastrointestinal infection suspected	Mesalamine (3 g/day) + cefixime (0.2 g/day)
Myocarditis (UC flare)	Trimetazidine and potassium and magnesium supplementation mesalamine (4 g/day) + hydrocortisone (100 mg q12h)

3) Was the patient received vaccine for SARS-CoV-2, recently?

He had not received vaccination against SARS-CoV-2 before admission, and this is now mentioned.

Responses to Reviewer 3

The authors present a case of a 15-year-old boy who presented with myocarditis as the initial presentation of a relapse of ulcerative colitis. Gastrointestinal symptoms of the patient were mild and he only had mild cardiac symptoms and minimal ventricular dysfunction except for acute chest pain, and therefore the authors propose that cardiovascular manifestations of IBD may be more common than clinically documented, since they may remain undiagnosed. This paper has been well written and the case is interesting. However, the author should address the following points.

1)Major 1. The authors described in the section of discussion that “mesalamine was administered over a long duration without steroids and there were no notable previous adverse cardiac events.”, “Our patient developed myocarditis after recovery from a gastrointestinal infection,”, but they are not shown in the section of case presentation. Thus, I suggest that the authors should describe history of past and present illness of the patient in more detail. 2.

Thank you for your positive feedback and suggestions, and we have refined the description of the history of past and present illness as follows:

“The boy had a two-year history of histologically-proven extensive UC, for which mesalamine was effective to achieve remission without adverse reactions. Two weeks prior to presentation, he experienced 7-8 bloody stools per day after eating ice cream, at which time he had been taking mesalamine (3 g/day) as maintenance therapy for a year. Given a likely gastrointestinal infection, cefixime (0.2 g/day) was added. His diarrhea and bloody stools improved quickly from 7-8 times a day to twice a day, which confirmed our diagnosis of infection. However, without any antibiotic changes, he developed

modest fever, progressive pleuritic chest pain, and shortness of breath after activity. There was no personal nor familial history of cardiac abnormality or dysfunction.”

2) I suggest that the authors should show the typical CMR findings of myocarditis as well as the criteria for diagnosis of myocarditis in detail. The authors also should explain the images of CMR in Figure 1 in an easy-to-understand manner with arrows.

A raised signal over 1300 ms in T1 and T2 sequences suggests acute myocarditis. As shown in our figure, the lesion is diffuse, so it is hard to identify very specific parts of the lesion, i.e., they were punctiform, quite small, but due to the lesions the T1 mapping signal was increased in the region of interest. We have added arrows to the images to show the abnormal sites for clarity.

3) Minor 1. The image quality of Fig. 2 (especially Fig. 2B) appears to be poor for detailed evaluation.

The figure is that obtained during the examination, but we have improved Figure 2B's quality in the revised version.

Responses to Reviewer 4

1) In this paper, the authors reported a 15-year-old boy who developed myocarditis as an extraintestinal manifestation (EIM) with the relapse of ulcerative colitis. They also reviewed the 21 patients with myocarditis associated with IBD that reported previously. As the authors described, myocarditis is very rare among the EIM of IBD. Thus, this paper has a clinical value. However, there are several problems to be reconsidered as follows. Comments) 1) Myocarditis in this patient developed consistent with the relapse of ulcerative colitis and improved consistent with the endoscopic improvement of ulcerative colitis. The authors should simply state that

point, without saying that there was a discrepancy with the symptoms. The tedious description makes it difficult to understand.

We have simplified the expression as follows: “During the improvement in gastrointestinal symptoms, our patient developed acute chest pain, which implied a UC flare as confirmed by colonoscopy. The bloody diarrhea was under control at that time, leading to difficulties in early diagnosis.”

2) In this patient, the presence or absence of a link between 5-ASA administration and myocarditis is important. Please state whether this drug was continuously administered during the improvement of myocarditis. The DLST result for 5-ASA should be presented.

- 1) We have now made it clear that mesalamine was used throughout the course of myocarditis treatment as follows:
“The patient was treated with mesalamine (4 g/day) and hydrocortisone (100 mg q12h), taking the mesalamine continuously during recovery from myocarditis.”
- 2) We did not perform a drug lymphocyte stimulation test, instead ruling out 5-ASA as a cause due to the long-term administration of mesalamine.

3) In this paper, the description about the evaluation of myocarditis is insufficient. Ejection fraction (EF) of echocardiography should be presented.

We have now presented the echo results in full and mentioned that the LVEF was 66%.

4) In cardiac MR images, it is necessary to indicate an arrow at the site of abnormal findings. It is difficult to understand as it is.

We have added arrows to indicate the sites of abnormal findings.

5) In discussion, the authors described; the incidence rate ratio for developing myocarditis is 8.3 for CD and 2.6 for UC compared to the background population. What is the unit? Is it %?

This had been modified as follows:

“The incidence rate ratio for developing myocarditis is 8.3-times for CD and 2.6-times for UC compared with the background population.”

Responses to Reviewer 5

The article entitled “Myocarditis as an extraintestinal manifestation of ulcerative colitis: A case report and literature review” have reported a rare case of ulcerative colitis with myocarditis as an extraintestinal manifestation. The case is certainly important and interesting, and seems to be worth reporting. The sentences are concise and easy to read. Major revision: There is no major revision. Minor revisions; Because diagnosis of myocarditis is difficult especially in an early stage, ECG and other cardiac enzymes, such as CK-MB or LDH, may help early diagnosis. So, please show these in case presentation.

Thank you for this positive feedback and suggestions. We have now added CK-MB and LDH results, which were normal, to the revised manuscript.

Responses to a re-reviewer

The manuscript has been significantly improved in the revised version.

Thank you for this positive feedback.